

# STN-Structure Search

10/553,532

10/31/06

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L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:693872 CAPLUS

DOCUMENT NUMBER: 145:284333

TITLE: Evaluation of indenoisoquinoline topoisomerase I inhibitors using a hollow fiber assay

AUTHOR(S): Morrell, Andrew; Jayaraman, Muthusamy; Nagarajan, Muthukaman; Fox, Brian M.; Meckley, Marantha Rae; Ioanoviciu, Alexandra; Pommier, Yves; Antony, Smitha; Hollingshead, Melinda; Cushman, Mark

CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular Pharmacology, Purdue Cancer Center, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, IN, 47907, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(16), 4395-4399

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

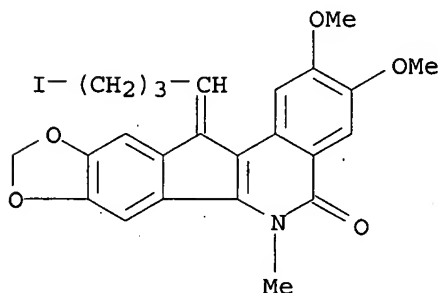
AB The indenoisoquinolines are a novel class of non-camptothecin topoisomerase I (Top1) inhibitors whose mechanism of action involves trapping the covalent complex formed between DNA and Top1 during cellular processes. As an ongoing evaluation of the indenoisoquinolines for Top1 inhibition and anticancer activity, indenoisoquinoline analogs have been screened in the National Cancer Institute's hollow fiber assay (HFA). Some of the derivs. demonstrated significant activity at i.p. and s.c. fiber placement sites, along with net cancer cell kill in one or more cell lines.

IT 907607-18-5

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(indenoisoquinoline topo I inhibitors screening and evaluation as antitumors)

RN 907607-18-5 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 6,12-dihydro-12-(4-iodobutylidene)-2,3-dimethoxy-6-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:318905 CAPLUS

DOCUMENT NUMBER: 144:363079

TITLE: Modulating MxA expression

INVENTOR(S): Trepel, Jane; Lin, Alexandra; Lee, Sunmin; Khanna, Chand; Lee, Min-Jung; Chung, Eun Joo; Covell, David

PATENT ASSIGNEE(S): Government of the United States of America as

Represented by the Secretary of the Department of  
Health and Human Services, USA  
SOURCE: PCT Int. Appl., 109 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006037052	A2	20060406	WO 2005-US34849	20050927
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2004-613371P P 20040927

OTHER SOURCE(S): MARPAT 144:363079

AB The invention provides comps. and methods for inhibiting cell motility, metastatic cancer and viral infections in a mammal that involve increasing the activity or expression of MxA. In some embodiments, the agent that can increase the expression of MxA is a compound of formula R1-X(R3)-R2 wherein: X is methylene (CH2), nitrogen or oxygen; R1 and R2 are cycloalkyl, aryl, arylalkylene, heteroaryl, heterocyclyl, or alkyl, any of which may be substituted with oxygen (O), hydroxy (OH), sulfite (SO3), sulfate (SO4), sulfonamide (NH-SO2 or NH-SO3), halogen (F, Cl, Br, or I), carboxylate (CO2), nitro (NO2), amino (NH2), secondary or tertiary alkylamino, alkylsulfonamide, lower alkyl, cycloalkyl, alkylenehydroxy, alkoxy, alkoxycarbonyl, alkoxyalkylenecarboxylic acid, alkylencarboxylic acid, alkyleneaminoalkylene, alkyleneaminoalkylenehydroxy, alkanoyloxy, aminoaryl or aryl; and R3 is nothing, hydrogen or, together with an X nitrogen to which it is attached, forms a heterocyclic ring with 0-2 double bonds between the carbon atoms of the heterocyclic ring or 0-1 addnl. nitrogen atoms. Another aspect of the invention is a method of treating or preventing cancer in a mammal by administering to the mammal a therapeutically effective amount of an MxA polypeptide or a nucleic acid encoding a MxA polypeptide.

IT 577705-02-3, NSC 717200

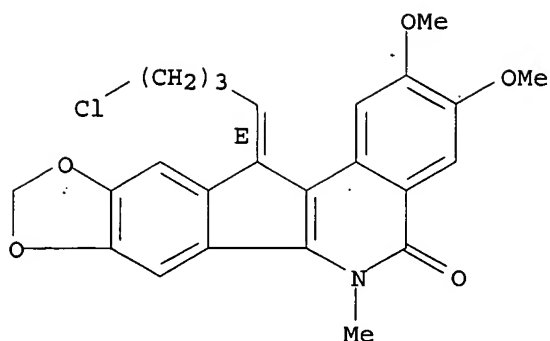
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(modulating MxA protein expression to inhibit cell motility and metastatic cancer and viral infections)

RN 577705-02-3 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 12-(4-chlorobutylidene)-6,12-dihydro-2,3-dimethoxy-6-methyl-, (12E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:76852 CAPLUS  
 DOCUMENT NUMBER: 144:143080  
 TITLE: Methods for treating or preventing erectile dysfunction or urinary incontinence  
 INVENTOR(S): Szabo, Csaba; Salzman, Andrew L.  
 PATENT ASSIGNEE(S): Inotek Pharmaceuticals Corporation, USA  
 SOURCE: PCT Int. Appl., 143 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006009718	A2	20060126	WO 2005-US21064	20050615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

US 2006019980	A1	20060126	US 2005-153628	20050615
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PRIORITY APPLN. INFO.:	US 2004-580040P	P	20040616
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OTHER SOURCE(S): MARPAT 144:143080

AB The present invention relates to methods for treating or preventing erectile dysfunction or urinary incontinence, comprising administering to a subject in need thereof an effective amount of a compound of the invention.

IT 501364-66-5P 501364-71-2P 501364-89-2P

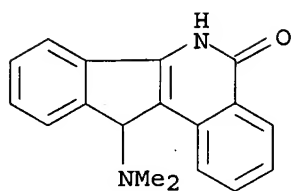
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(comps. for treating or preventing erectile dysfunction or urinary incontinence)

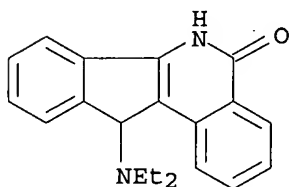
RN 501364-66-5 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(dimethylamino)-6,11-dihydro- (9CI)  
 (CA INDEX NAME)

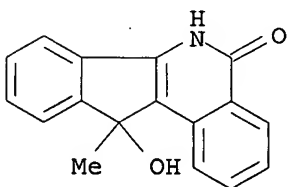
10/553,532



RN 501364-71-2 CAPLUS  
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(diethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)



RN 501364-89-2 CAPLUS  
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-11-methyl-  
(9CI) (CA INDEX NAME)

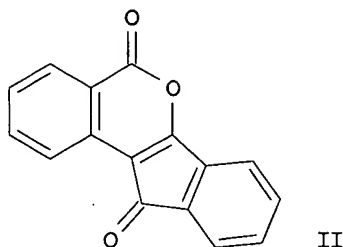
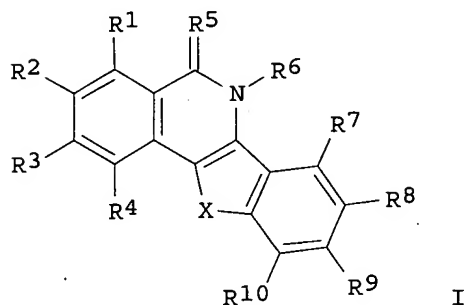


L4 . ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:984028 CAPLUS  
DOCUMENT NUMBER: 143:286298  
TITLE: Preparation of isoquinoline derivatives as PARS  
inhibitors  
INVENTOR(S): Jagtap, Prakash; Baloglu, Erkan; Van Duzer, John H.;  
Szabo, Csaba; Salzman, Andrew L.; Roy, Aloka;  
Williams, William; Nivorozhkin, Alexander  
PATENT ASSIGNEE(S): Inotek Pharmaceuticals Corporation, USA  
SOURCE: PCT Int. Appl., 158 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082368	A1	20050909	WO 2005-US6243	20050225
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,				

SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG

US 2005228007 A1 20051013 US 2005-66824 20050225  
 PRIORITY APPLN. INFO.: US 2004-547899P P 20040226  
 OTHER SOURCE(S): MARPAT 143:286298  
 GI



AB The present invention relates to isoquinoline derivs. I [R5 = O, NH, S; R6 = H, alkyl; X = CO, CH2, CH(halo), etc.; R1 = H, halo, alkyl, etc.; R2-R4, R7-R10 = H, halo, OH, etc.], compns. comprising an effective amount of I and methods for treating or preventing an inflammatory disease, a reperfusion injury, an ischemic condition, renal failure, diabetes, a diabetic complication, a vascular disease other than a cardiovascular disease, cardiovascular disease, reoxygenation injury resulting from organ transplantation, Parkinson's disease, or cancer, comprising administering to an animal in need thereof an effective amount of the compound I.

#### Preparation of

illustrative isoquinolines I is described in examples. E.g., a multi-step synthesis of I [R5 = O; R1-R4, R6-R8, R10 = H; R9 = SO2NH(CH2)3(morpholin-4-yl); X = CH2] and its mesylate salt, starting from II, was given. The exemplified above compound I and its mesylate salt were tested in various tests. For example, the mesylate salt exerted 50% inhibition of PARS activity at 3 nM and thus was approx. 50,000 times more potent than the reference compound 3-aminobenzamide.

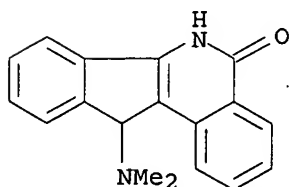
IT 501364-66-5P 501364-71-2P 501364-89-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of isoquinoline derivs. as PARS inhibitors)

RN 501364-66-5 CAPLUS

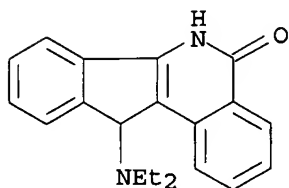
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(dimethylamino)-6,11-dihydro- (9CI)  
 (CA INDEX NAME)



RN 501364-71-2 CAPLUS

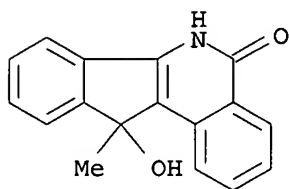
10/553,532

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(diethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)



RN 501364-89-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-11-methyl-  
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:286165 CAPLUS

DOCUMENT NUMBER: 142:423066

TITLE: On the Binding of Indeno[1,2-c]isoquinolines in the  
DNA-Topoisomerase I Cleavage Complex

AUTHOR(S): Xiao, Xiangshu; Antony, Smitha; Pommier, Yves;  
Cushman, Mark

CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular  
Pharmacology and the Purdue Cancer Center School of  
Pharmacy and Pharmaceutical Sciences, Purdue  
University, West Lafayette, IN, 47907, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(9),  
3231-3238

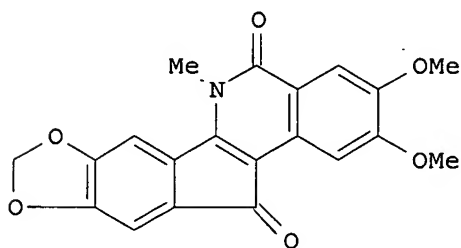
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB An ab initio quantum mechanics calcn. is reported which predicts the

orientation of indenoisoquinoline (I) in the ternary cleavage complex formed from DNA and topoisomerase I (top1). The results of this calcn. are consistent with the hypothetical structures previously proposed for the indenoisoquinoline-DNA-top1 ternary complexes based on mol. modeling, the crystal structure of a recently reported ternary complex, and the biol. results obtained with a pair of diaminoalkyl-substituted indenoisoquinoline enantiomers. The results of these studies indicate that the  $\pi$ - $\pi$  stacking interactions between the indenoisoquinolines and the neighboring DNA base pairs play a major role in determining binding orientation. The calcn. of the electrostatic potential surface maps of the indenoisoquinolines and the adjacent DNA base pairs shows electrostatic complementarity in the observed binding orientation, leading to the conclusion that electrostatic attraction between the intercalators and the base pairs in the cleavage complex plays a major stabilizing role. On the other hand, the calcn. of LUMO and HOMO energies of indenoisoquinoline II and neighboring DNA base pairs in conjunction with NBO anal. indicates that charge transfer complex formation plays a relatively minor role in stabilizing the ternary complexes derived from indenoisoquinolines, DNA, and top1. The results of these studies are important in understanding the existing structure-activity relationships for the indenoisoquinolines as top1 inhibitors and as anticancer agents, and they will be important in the future design of indenoisoquinoline-based top1 inhibitors.

IT 761456-71-7P 850723-29-4P

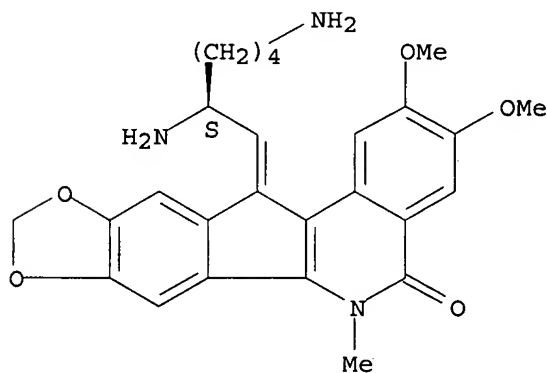
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(binding of indeno[1,2-c]isoquinolines in DNA-topoisomerase I cleavage complex)

RN 761456-71-7 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 12-[(2S)-2,6-diaminohexylidene]-6,12-dihydro-2,3-dimethoxy-6-methyl- (9CI) (CA INDEX NAME)

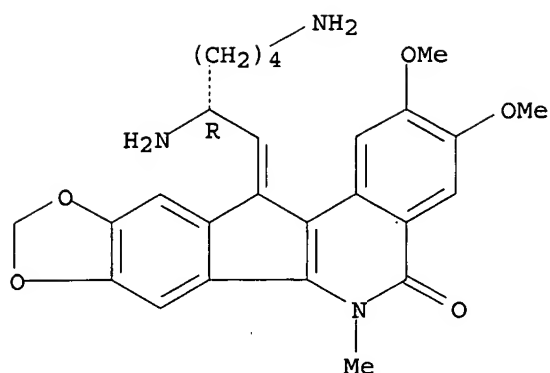
Absolute stereochemistry.  
Double bond geometry unknown.



RN 850723-29-4 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 12-[(2R)-2,6-diaminohexylidene]-6,12-dihydro-2,3-dimethoxy-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

*Answers*  
 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:1015857 CAPLUS  
 DOCUMENT NUMBER: 142:6424  
 TITLE: Preparation of indeno and isoindoloisoquinolone derivatives as cytotoxic agents  
 INVENTOR(S): Cushman, Mark S.; Pommier, Yves G.  
 PATENT ASSIGNEE(S): Purdue Research Foundation, USA; The Government of the United States of America as Represented by the Department of Health and Human Services  
 SOURCE: PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

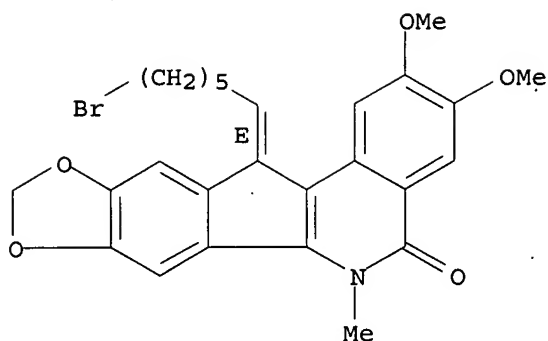
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100891	A2	20041125	WO 2004-US14581	20040511
WO 2004100891	A3	20050414		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004238329	A1	20041125	AU 2004-238329	20040511
CA 2525099	AA	20041125	CA 2004-2525099	20040511
EP 1646388	A2	20060419	EP 2004-760968	20040511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-469718P P 20030512  
 WO 2004-US14581 W 20040511

OTHER SOURCE(S): MARPAT 142:6424  
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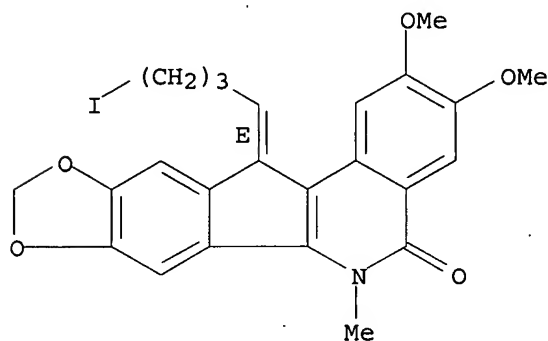
10/553,532



RN 577705-06-7 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 6,12-dihydro-12-(4-iodobutylidene)-2,3-dimethoxy-6-methyl-, (12E)- (9CI) (CA INDEX NAME)

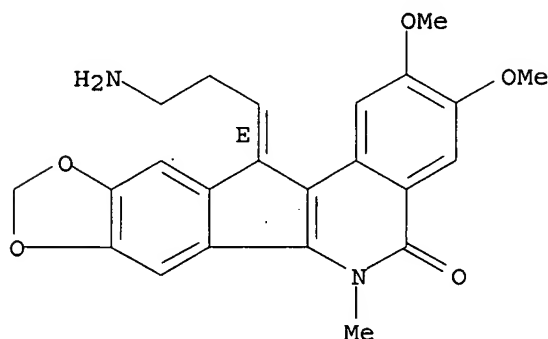
Double bond geometry as shown.



RN 577705-07-8 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 12-(3-aminopropylidene)-6,12-dihydro-2,3-dimethoxy-6-methyl-, (12E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L4 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

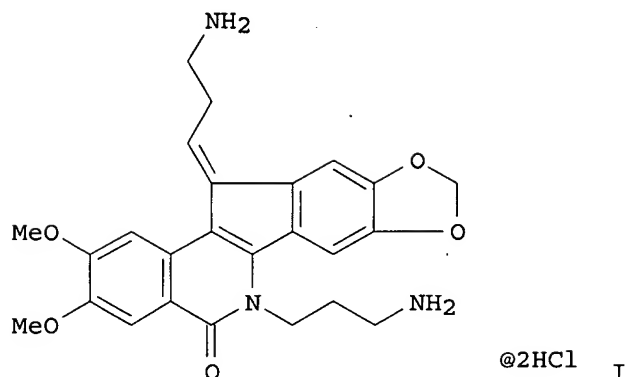
ACCESSION NUMBER: 2004:795350 CAPLUS

DOCUMENT NUMBER: 141:424101

TITLE: Novel Autoxidative Cleavage Reaction of 9-Fluorenes  
Discovered during Synthesis of a Potential  
DNA-Threading Indenoisoquinoline

10/553,532

AUTHOR(S): Xiao, Xiangshu; Antony, Smitha; Kohlhagen, Glenda;  
Pommier, Yves; Cushman, Mark  
CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular  
Pharmacology, School of Pharmacy and Pharmacal  
Sciences, Purdue University, West Lafayette, IN,  
47907, USA  
SOURCE: Journal of Organic Chemistry (2004), 69(22), 7495-7501  
CODEN: JOCEAH; ISSN: 0022-3263  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 141:424101  
GI



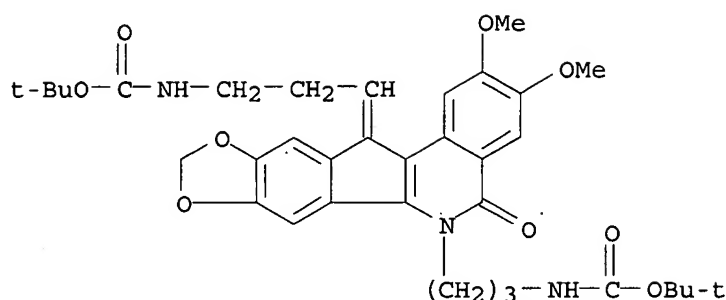
AB The indenoisoquinolines are a novel class of cytotoxic non-camptothecin topoisomerase I inhibitors. A potential DNA-threading agent was designed by attaching different amine side chains on the lactam nitrogen as well as on the C11 position of the indenoisoquinoline ring system. It was hypothesized that substituents on the lactam nitrogen could protrude out toward the DNA major groove while those on the C11 project out toward the DNA minor groove in the ternary "cleavage complex.". Compound I was synthesized in order to test this DNA-threading scenario. It was found unexpectedly that an alkenyl substituent on the C11 position was autoxidatively cleaved under basic conditions to afford a ketone. A possible mechanism for this unusual oxidative cleavage was proposed on the basis of the studies of a 9-fluorenone model compound. The proposed mechanism was further supported by computational studies. Although the designed compound I showed potent cytotoxicities in various cancer cell lines, it was less potent than its nonthreading counterparts and was not a topoisomerase I inhibitor.

IT 795311-68-1

RL: PRP (Properties)  
(acidity and mol. structure of)

RN 795311-68-1 CAPLUS

CN 5H-1,3-Dioxolo[4,5-g][1,3]dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one,  
12-ethylidene-6,12-dihydro-6-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:735311 CAPLUS

DOCUMENT NUMBER: 141:288560

TITLE: Design, synthesis, and biological evaluation of cytotoxic 11-aminoalkenylindenoisoquinoline and 11-diaminoalkenylindenoisoquinoline topoisomerase I inhibitors

AUTHOR(S): Xiao, Xiangshu; Antony, Smitha; Kohlhagen, Glenda; Pommier, Yves; Cushman, Mark

CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN, 47907, USA

SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(19), 5147-5160

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:288560

AB The cytotoxic indenoisoquinolines are a novel class of noncamptothecin topoisomerase I inhibitors having certain features that compare favorably with the camptothecins. A new strategy was adopted to attach aminoalkenyl substituents at C-11 of the indenoisoquinoline ring system, which, according to mol. modeling, would orient the side chains toward the DNA minor groove. All of the newly synthesized compds. were more cytotoxic than the parent indenoisoquinoline NSC 314622. Despite an imperfect correlation between cytotoxicities and topoisomerase I inhibition results, the hypothetical structural model of the cleavage complex presented here provides a conceptual framework to explain the structure-activity relationships.

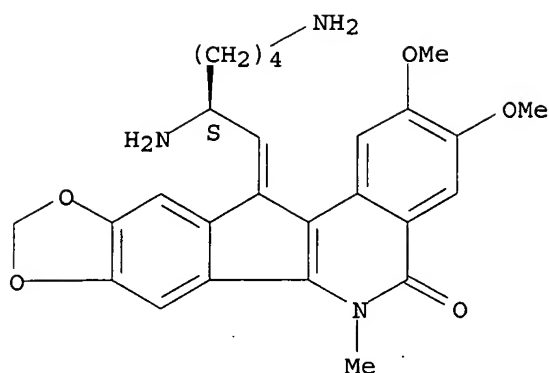
IT 761456-59-1

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(design and synthesis and biol. evaluation of cytotoxic 11-aminoalkenylindenoisoquinoline and 11-diaminoalkenylindenoisoquinoline topoisomerase I inhibitors in relation to suppression of DNA cleavage)

RN 761456-59-1 CAPLUS

CN 5H-[1,3]Dioxolo[5,6]indeno[1,2-c]isoquinolin-5-one, 12-(3-aminopropylidene)-6,12-dihydro-2,3-dimethoxy-6-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:162464 CAPLUS

DOCUMENT NUMBER: 140:217625

TITLE: Preparation of substituted indenoisoquinolinones, indoloisoquinolinones and oxa(thia)azabenzofluorenones for the treatment of inflammatory disease or reperfusion disease

INVENTOR(S): Jagtap, Prakash; Baloglu, Erkan; Van Duzer, John H.; Szabo, Csaba; Salzman, Andrew L.; Roy, Aloka; Williams, William; Nivoroshkin, Alexander

PATENT ASSIGNEE(S): Inotek Pharmaceuticals Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 233,198.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

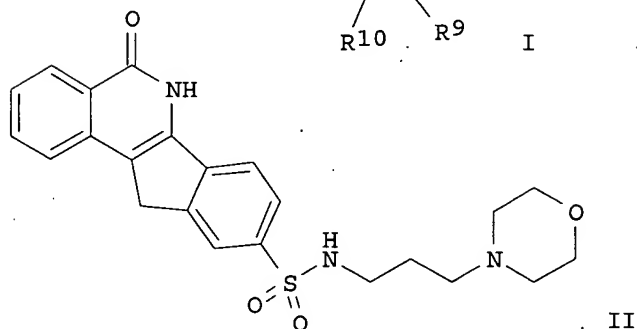
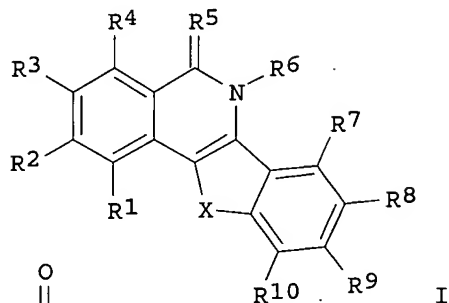
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004039009	A1	20040226	US 2003-376746	20030228
US 6956035	B2	20051018		
US 2003096833	A1	20030522	US 2001-944524	20010831
US 2003171392	A1	20030911	US 2002-233198	20020830
US 6828319	B2	20041207		
AU 2004218023	A1	20040916	AU 2004-218023	20040226
CA 2517358	AA	20040916	CA 2004-2517358	20040226
WO 2004078712	A2	20040916	WO 2004-US5849	20040226
WO 2004078712	A3	20050224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1603568	A2	20051214	EP 2004-715130	20040226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007922	A	20060301	BR 2004-7922	20040226
CN 1780625	A	20060531	CN 2004-80011423	20040226
JP 2006520817	T2	20060914	JP 2006-508867	20040226

10/553,532

US 2005049270	A1	20050303	US 2004-963293	20041012
US 2005282848	A1	20051222	US 2005-177161	20050708
PRIORITY APPLN. INFO.:			US 2001-944524	B2 20010831
			US 2002-233198	A2 20020830
			US 2003-376746	A 20030228
			WO 2004-US5849	A 20040226

OTHER SOURCE(S):            MARPAT 140:217625

GI

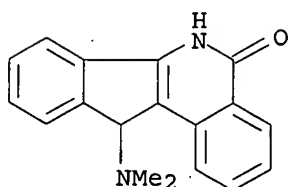


AB The title compds. [I; X = CO, CH<sub>2</sub>, CH(halo), O, NH, S, etc.; R<sub>1</sub> = H, halo, alkyl, etc.; R<sub>2</sub>-R<sub>4</sub>, R<sub>7</sub>-R<sub>10</sub> = H, halo, OH, alkoxy, aryl, NH<sub>2</sub>, etc.; R<sub>5</sub> = O, NH, S; R<sub>6</sub> = H, alkyl] were prepared for treating or preventing inflammatory disease or reperfusion disease. Thus, II was prepared and showed 84% poly(ADP-ribose) synthase inhibition at 300 nM. The pharmaceutical composition comprising the compound I is claimed.

IT 501364-66-5P 501364-71-2P 501364-89-2P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of indenoisoquinolinones, indoloisoquinolinones and oxa(thia)azabenzofluorenones for the treatment of inflammatory disease or reperfusion disease)

RN 501364-66-5 CAPLUS

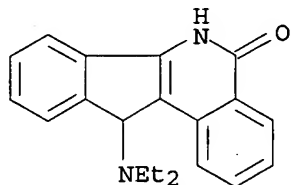
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(dimethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)



10/553,532

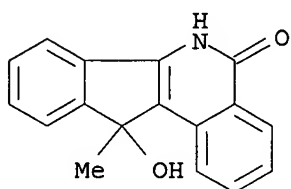
RN 501364-71-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(diethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)



RN 501364-89-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-11-methyl-  
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:717759 CAPLUS

DOCUMENT NUMBER: 139:230633

TITLE: Preparation of substituted indeno[1,2-c]isoquinoline  
derivatives for the treatment of inflammatory disease  
or reperfusion disease

INVENTOR(S): Jagtap, Prakash; Baloglu, Erkan; Van Duzer, John H.;  
Szabo, Csaba; Salzman, Andrew L.

PATENT ASSIGNEE(S): Inotek Pharmaceuticals Corp., USA

SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S.  
Ser. No. 944,524.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

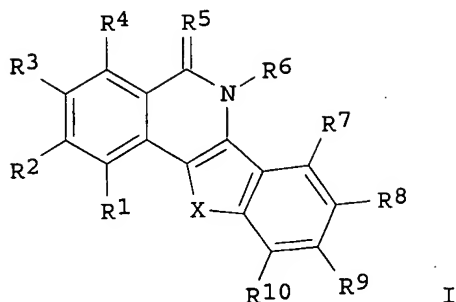
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003171392	A1	20030911	US 2002-233198	20020830
US 6828319	B2	20041207		
US 2003096833	A1	20030522	US 2001-944524	20010831
CN 1575172	A	20050202	CN 2002-821325	20020830
US 2004039009	A1	20040226	US 2003-376746	20030228
US 6956035	B2	20051018		
ZA 2004001376	A	20041119	ZA 2004-1376	20040219
US 2005049270	A1	20050303	US 2004-963293	20041012
US 2005282848	A1	20051222	US 2005-177161	20050708
PRIORITY APPLN. INFO.:			US 2001-944524	A2 20010831
			US 2002-233198	A2 20020830
			US 2003-376746	A3 20030228

OTHER SOURCE(S): MARPAT 139:230633

10/553,532

GI



AB Novel indeno[1,2-c]isoquinoline derivs. of formula I [X = CO, CH<sub>2</sub>, CH(halo), O, NH, S, etc.; R<sub>1</sub>-R<sub>4</sub>, R<sub>7</sub>-R<sub>10</sub> = H, halo, OH, alkoxy, aryl, NH<sub>2</sub>, etc.; R<sub>5</sub> = NH, S; R<sub>6</sub> = H, alkyl] are prepared for treating or preventing inflammatory disease or reperfusion disease. Thus, 5,6-dihydro-5,11-diketo-11H-indeno[1,2-c]isoquinoline prepared by refluxing a suspension of benz[d]indeno[1,2-b]pyran-5,11-dione in NH<sub>3</sub>/MeOH for 24 h; cooling, filtering; and washing was tested for inhibitory effect on PARS activation in cultured murine macrophages and showed 60% PARS inhibition at 1 μM.

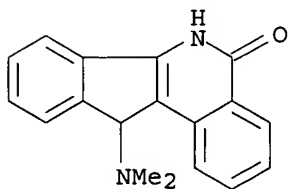
IT 501364-66-5P 501364-71-2P 501364-89-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indenoisoquinoline derivs. for the treatment of inflammatory disease or reperfusion disease)

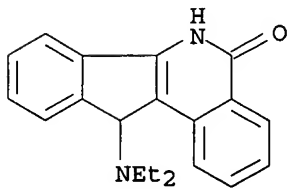
RN 501364-66-5 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(dimethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)



RN 501364-71-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(diethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)

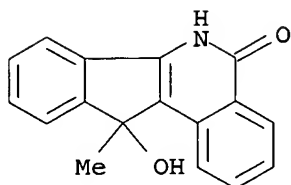


RN 501364-89-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-11-methyl-

10/553,532

(9CI) (CA INDEX NAME)



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:459815 CAPLUS

DOCUMENT NUMBER: 139:164721

TITLE: Design, Synthesis, and Biological Evaluation of Cytotoxic 11-Alkenylindenoisoquinoline Topoisomerase I Inhibitors and Indenoisoquinoline-Camptothecin Hybrids  
AUTHOR(S): Fox, Brian M.; Xiao, Xiangshu; Antony, Smitha; Kohlhausen, Glenda; Pommier, Yves; Staker, Bart L.; Stewart, Lance; Cushman, Mark

CORPORATE SOURCE: Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN, 47907, USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(15), 3275-3282

CODEN: JMCMAR; ISSN: 0022-2623

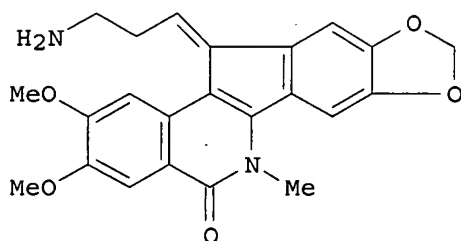
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:164721

GI



I

AB The indenoisoquinolines are a novel class of topoisomerase I (top1) inhibitors that are cytotoxic in cancer cell cultures and are therefore under development as potential anticancer agents. As inhibitors of the DNA religation reaction occurring after DNA cleavage by the enzyme, they are classified as top1 poisons, similar to the camptothecins. Two strategies were employed in order to further develop the structure-activity relationships of the indenoisoquinolines and enhance their therapeutic potential. The first strategy involved the synthesis of indenoisoquinoline-camptothecin hybrid mols. to take advantage of a proposed structural analogy between the indenoisoquinolines and camptothecin. The desired hybrids were synthesized by reaction of halogenated phthalides with a dihydropyrroloquinoline. The second strategy involved the attachment of various alkenyl substituents to the



C-11 position of the indenoisoquinolines, which were assumed to project into the DNA minor groove. The required C-11-substituted indenoisoquinolines were synthesized by McMurry reactions of 11-ketoindenoisoquinolines with aldehydes, and the geometries of the resulting alkenes were established by nuclear Overhauser effect difference NMR spectroscopy. All of the new indenoisoquinolines were examined for cytotoxicity in human cancer cell cultures as well as for activity vs top1. Although the indenoisoquinoline-camptothecin hybrid mols. proved to be less cytotoxic and displayed less activity against top1, the analog I, incorporating a 3'-aminoalkenyl substituent at the C-11 position of the indenoisoquinoline system, was significantly more potent than the prototype indenoisoquinoline in both assays. These results indicate that C-11 aminoalkyl substituents that are assumed to project into the minor groove enhance the cytotoxicity and top1 inhibitory activity of the parent indenoisoquinoline system.

IT 577705-08-9 577705-09-0

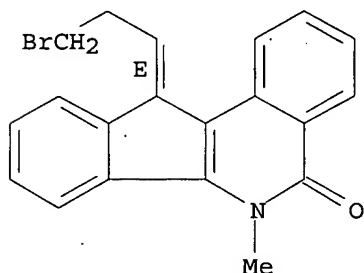
RL: PRP (Properties)

(calculated global min. energy of)

RN 577705-08-9 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(3-bromopropylidene)-6,11-dihydro-6-methyl-, (11E)- (9CI) (CA INDEX NAME)

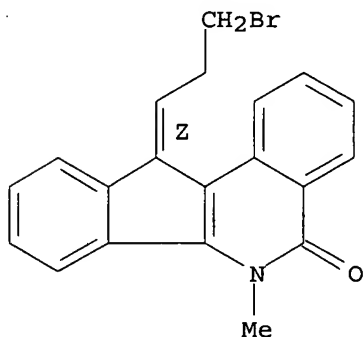
Double bond geometry as shown.



RN 577705-09-0 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(3-bromopropylidene)-6,11-dihydro-6-methyl-, (11Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

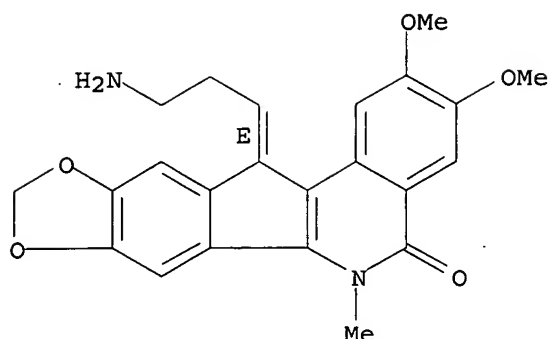


IT 577705-03-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 11-alkylideneindenoisoquinolines as topoisomerase I inhibitors and indenoisoquinoline-camptothecin hybrids)

RN 577705-03-4 CAPLUS



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:202622 CAPLUS

DOCUMENT NUMBER: 138:238028

TITLE: Preparation of substituted indeno[1,2-c]isoquinoline derivatives for the treatment of inflammatory disease or reperfusion disease

INVENTOR(S): Jagtap, Prakash G.; Baloglu, Erkan; Van Duzer, John H.; Szabo, Csaba; Salzman, Andrew L.

PATENT ASSIGNEE(S): Inotek Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

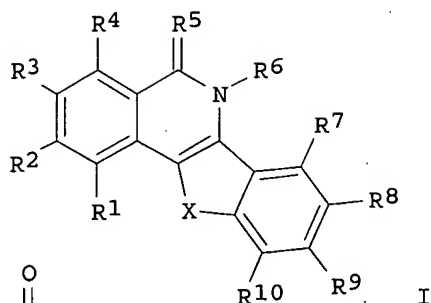
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

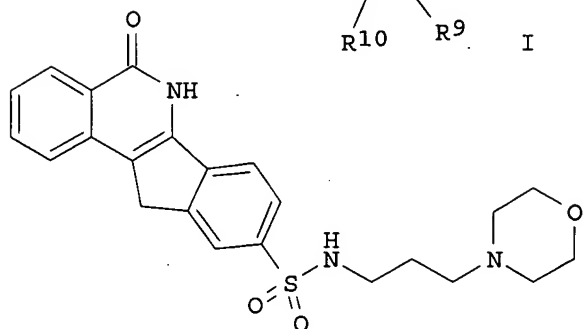
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020700	A2	20030313	WO 2002-US27585	20020830
WO 2003020700	A3	20040212		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003096833	A1	20030522	US 2001-944524	20010831
CA 2457534	AA	20030313	CA 2002-2457534	20020830
EP 1420785	A2	20040526	EP 2002-766175	20020830
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002012225	A	20050118	BR 2002-12225	20020830
JP 2005502681	T2	20050127	JP 2003-524971	20020830
CN 1575172	A	20050202	CN 2002-821325	20020830
NZ 531218	A	20060224	NZ 2002-531218	20020830
ZA 2004001376	A	20041119	ZA 2004-1376	20040219
NO 2004000845	A	20040401	NO 2004-845	20040226
PRIORITY APPLN. INFO.:			US 2001-944524	A 20010831
			WO 2002-US27585	W 20020830

OTHER SOURCE(S): MARPAT 138:238028

GI



I



II

AB Novel indeno[1,2-c]isoquinoline derivs. of formula I [X = CO, CH<sub>2</sub>, CH(halo), O, NH, S, etc.; R<sub>1</sub>-R<sub>4</sub>, R<sub>7</sub>-R<sub>10</sub> = H, halo, OH, alkoxy, aryl, NH<sub>2</sub>, etc.; R<sub>5</sub> = O, NH, S; R<sub>6</sub> = H, alkyl] are prepared for treating or preventing inflammatory disease or reperfusion disease. Thus, II was prepared and inhibited poly(ADP-ribose) synthase 84% at 300nM.

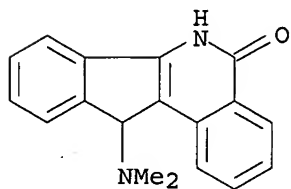
IT 501364-66-5P 501364-71-2P 501364-89-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indenoisoquinoline derivs. for the treatment of inflammatory disease or reperfusion disease)

RN 501364-66-5 CAPLUS

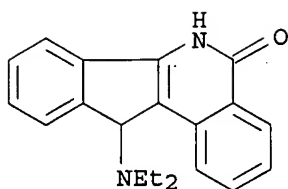
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(dimethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)



RN 501364-71-2 CAPLUS

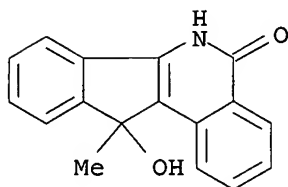
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 11-(diethylamino)-6,11-dihydro- (9CI)  
(CA INDEX NAME)

10/553,532



RN 501364-89-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-11-methyl-  
(9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:399108 CAPLUS

DOCUMENT NUMBER: 131:243440

TITLE: A novel synthesis of benzo[c]phenanthridine skeleton  
and biological evaluation of isoquinoline derivatives  
AUTHOR(S): Cho, Won-Jea; Park, Myun-Ji; Imanishi, Takeshi; Chung,  
Byung-Ho

CORPORATE SOURCE: College of Pharmacy, Chonnam National University,  
Kwangju, 500-757, S. Korea

SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(6),  
900-902

CODEN: CPBTAL; ISSN: 0009-2363

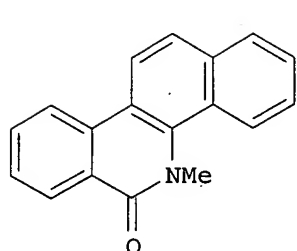
PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

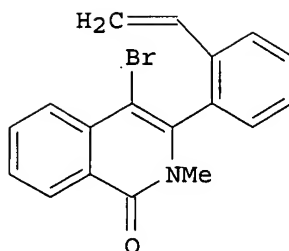
LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:243440

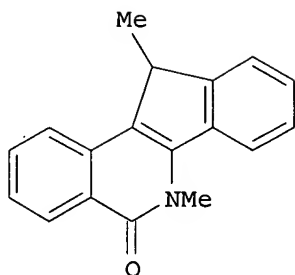
GI



I



II



III

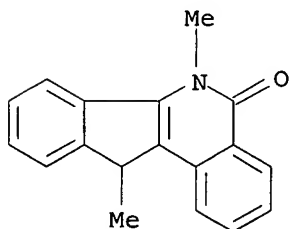
AB Benzo[c]phenanthridine skeleton I was synthesized from easily available starting N-methyl-o-toluidine and o-methylbenzonitrile in 7 steps. Radical cyclization of styrene II afforded 6,11-dimethyl-6,11-dihydro-5H-indeno[1,2-c]isoquinolin-5-one III. Most 3-arylisoquinolines have displayed strong activities against human tumor cell lines. Especially, indenoisoquinolinone III exhibited excellent cytotoxicity (IC<sub>50</sub>=0.002 µg/mL; HCT 15).

IT 244128-30-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis of benzo[c]phenanthridine skeleton and biol. evaluation of isoquinoline derivs.)

RN 244128-30-1 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-6,11-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:269393 CAPLUS

DOCUMENT NUMBER: 130:352179

TITLE: Applications of carbon-nitrogen bond cleavage reaction: a synthesis/derivatization of 11H-indeno[1,2-c]isoquinolines

AUTHOR(S): Lal, Bansil; Gidwani, Ramesh M.

10/553,532

CORPORATE SOURCE: Research Center, Hoechst Marion Roussel Limited,  
Mumbai, 400 080, India

SOURCE: Indian Journal of Chemistry, Section B: Organic  
Chemistry Including Medicinal Chemistry (1999),  
38B(1), 33-39  
CODEN: IJSBDB; ISSN: 0376-4699

PUBLISHER: National Institute of Science Communication, CSIR

DOCUMENT TYPE: Journal

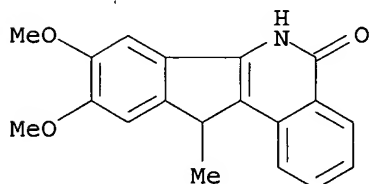
LANGUAGE: English

AB Orthophosphoric acid/HCOOH treatment of 3-(4,5-dimethoxy-2-vinylphenyl)-  
1(2H)-isoquinolinone and 6,7-dimethoxy 3-(4,5-dimethoxy-2-vinylphenyl)-  
1(2H)-isoquinolinone brings about cyclization to give the  
indeno[1,2-c]isoquinolines. Reaction with POCl<sub>3</sub> produces chloro compds.  
Hydrogenolysis gives dechlorinated products. Reaction of chloro derivs.  
with different amines gives amino substituted 11H-indeno-[1,2-  
c]isoquinolines.

IT 225218-16-6P 225218-17-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reactions of indenoisoquinolines)

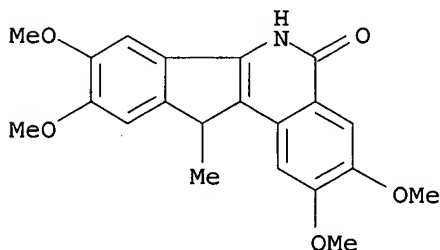
RN 225218-16-6 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-8,9-dimethoxy-11-methyl-  
(9CI) (CA INDEX NAME)



RN 225218-17-7 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-11-  
methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:174490 CAPLUS

DOCUMENT NUMBER: 116:174490

TITLE: Benzophenanthridines. XVI. Structural analogs.  
Reaction of 5,11-dimethyl-2,3,8,9-tetramethoxy-11H-  
indeno[1,2-c]isoquinolone with sodium hydride

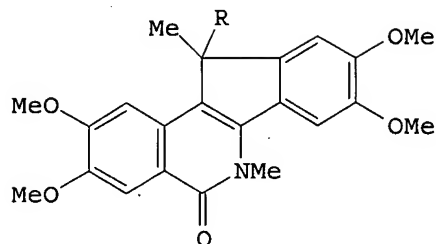
AUTHOR(S): Sazonova, N. M.; Levina, I. I.; Sladkov, V. I.;  
Suvorov, N. N.

CORPORATE SOURCE: Mosk. Khim.-Tekhnol. Inst., Moscow, USSR

SOURCE: Zhurnal Organicheskoi Khimii (1991), 27(10), 2223-6

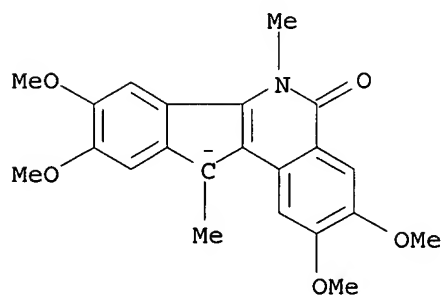
DOCUMENT TYPE:  
LANGUAGE:  
GI

Journal  
Russian



I

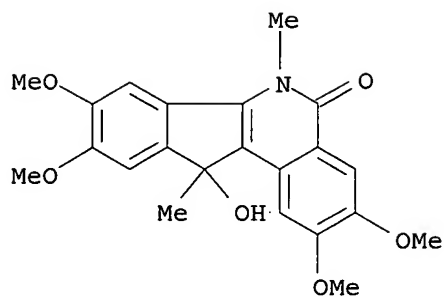
- AB The mechanism of reduction of the title compound I (R = H) was studied. The reduction with NaH generated the anion of I (R = Na), which then underwent an atmospheric air oxidation to afford the unusual product I (R = OH).
- IT 140169-40-0P  
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(formation and air oxidation of)
- RN 140169-40-0 CAPLUS
- CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-6,11-dimethyl-, ion(1-), sodium (9CI) (CA INDEX NAME)



● Na<sup>+</sup>

- IT 136540-28-8P  
RL: FORM (Formation, nonpreparative); PREP (Preparation)  
(formation of, in reduction of dimethyltetramethoxyindenoisoquinolone with sodium hydride)
- RN 136540-28-8 CAPLUS
- CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-2,3,8,9-tetramethoxy-6,11-dimethyl- (9CI) (CA INDEX NAME)

10/553,532

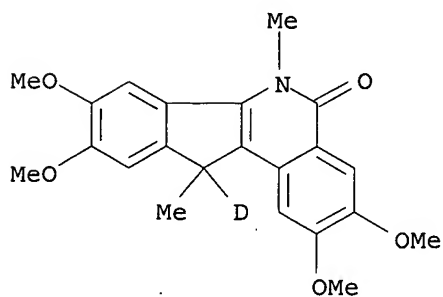


IT 140169-41-1P 140169-42-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

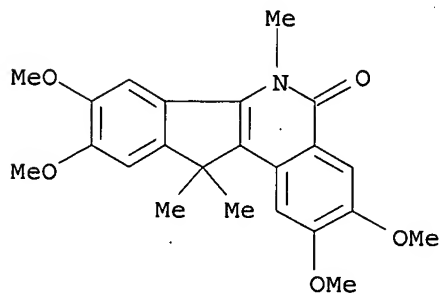
RN 140169-41-1 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one-11-d, 6,11-dihydro-2,3,8,9-tetramethoxy-  
6,11-dimethyl- (9CI) (CA INDEX NAME)



RN 140169-42-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-  
6,11,11-trimethyl- (9CI) (CA INDEX NAME)



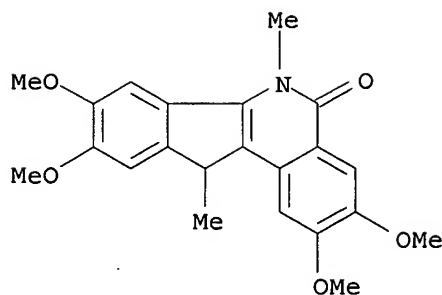
IT 125455-90-5

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reduction of, with lithiumaluminum hydride or sodium hydride, mechanism  
of)

RN 125455-90-5 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-6,11-  
dimethyl- (9CI) (CA INDEX NAME)





L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:583640 CAPLUS

DOCUMENT NUMBER: 115:183640

TITLE: Synthesis and antitumor activity of salts of O-methylfagaronine and its analog C-norbenzo[c]phenanthridine

AUTHOR(S): Sazonova, N. M.; Levina, I. I.; Bezrukov, I. A.; Ershova, Yu. A.; Sladkov, V. I.; Safonova, T. S.; Suvorov, N. N.

CORPORATE SOURCE: Mosk. Khim.-Tekhnol. Inst., Moscow, USSR

SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1991), 25(7), 31-4  
CODEN: KHFZAN; ISSN: 0023-1134

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Syntheses and antitumor activities of 5-methyl-2,3,8,9-tetramethoxybenzo[c]phenanthridine iodide and chloride and the structural analogs, 5,11-dimethyl-2,3,8,9-tetramethoxy-11H-indeno[1,2-c]isoquinoline, 5,11-dimethyl-2,3,8,9-tetramethoxy-11H-indeno[1,2-c]isoquinolinium chloride and 11-hydroxy-5,11-dimethyl-2,3,8,9-tetramethoxy-11H-indeno[1,2-c]isoquinolone were carried out. All the compds. showed weak antitumor and antileukemic activities. 5-Methyl-2,3,8,9-tetramethoxybenzo[c]phenanthridine iodide had the highest activity against leukemia P388, whereas 5,11-dimethyl-2,3,8,9-tetramethoxy-11H-indeno[1,2-c]isoquinolone had the highest activity against leukemia L1210.

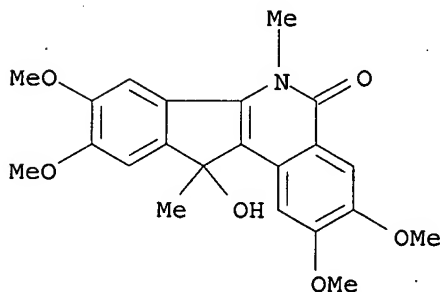
IT 136540-28-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and antileukemic activity of)

RN 136540-28-8 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-11-hydroxy-2,3,8,9-tetramethoxy-6,11-dimethyl- (9CI) (CA INDEX NAME)



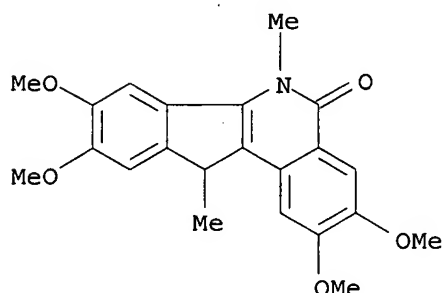
IT 125455-90-5P

10/553,532

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (preparation, quaternization, and antileukemic activity of)

RN 125455-90-5 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-6,11-dimethyl- (9CI) (CA INDEX NAME)

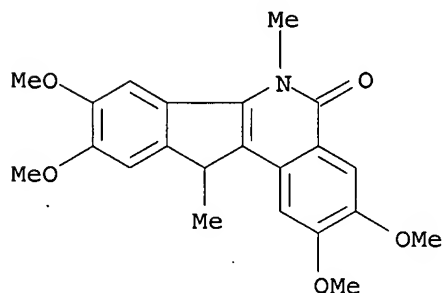


IT 136540-27-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (preparation, reactions, and antileukemic activity of)

RN 136540-27-7 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-6,11-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:61903 CAPLUS

DOCUMENT NUMBER: 114:61903

TITLE: New methodology for the preparation of the indeno[1,2-c]isoquinoline derivatives

AUTHOR(S): Gomes, Louis Mavoungou; Duval, Olivier

CORPORATE SOURCE: Lab. Chim. Org., UFR Med. Pharm., Angers., 49100, Fr.

SOURCE: Comptes Rendus de l'Academie des Sciences, Serie II: Mecanique, Physique, Chimie, Sciences de la Terre et de l'Univers (1990), 310(11), 1431-5

CODEN: CRAMED; ISSN: 0764-4450

DOCUMENT TYPE: Journal

LANGUAGE: French

10/553,532

OTHER SOURCE(S) : CASREACT 114:61903  
GI

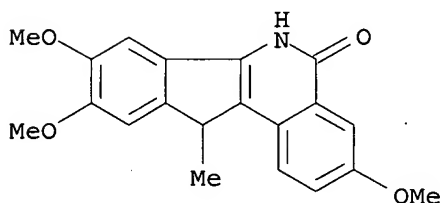
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The cycloaddn. of 2-(2-furyl)-5,6-dimethoxy-3-methyl-2,3-dihydro-1-indanone with di-Me acetylenedicarboxylate gives the dienic adduct I which is aromatized to the phthalic acid derivative and further O-methylated, hydrolyzed in alkaline solution and dehydrated to give anhydride II. Lactamization of II is realized either in the presence of ammonium or methylammonium acetate in anhydrous acetic acid medium or via refluxing the decarboxylated and lactonized product obtained from II in benzylamine. Indeno[1,2-c]isoquinolones III (R = CO<sub>2</sub>H, R<sub>1</sub> = H; R = H, R<sub>1</sub> = PhCH<sub>2</sub>) are then isolated.

IT 131673-93-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and chlorination of)

RN 131673-93-3 CAPLUS

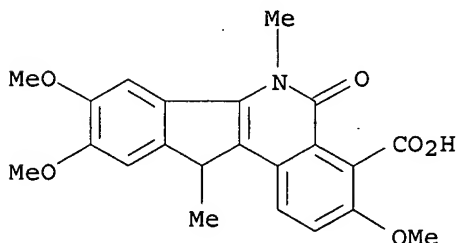
CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-3,8,9-trimethoxy-11-methyl- (9CI) (CA INDEX NAME)



IT 131673-68-2P 131673-91-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 131673-68-2 CAPLUS

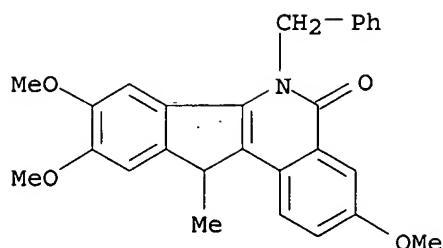
CN 5H-Indeno[1,2-c]isoquinoline-4-carboxylic acid, 6,11-dihydro-3,8,9-trimethoxy-6,11-dimethyl-5-oxo- (9CI) (CA INDEX NAME)



RN 131673-91-1 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-3,8,9-trimethoxy-11-methyl-6-(phenylmethyl)- (9CI) (CA INDEX NAME)

10/553,532

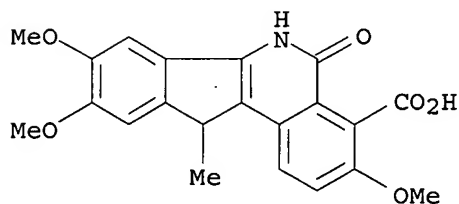


IT 131673-92-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation, lactamization, and decarboxylation of)

RN 131673-92-2 CAPLUS

CN 5H-Indeno[1,2-c]isoquinoline-4-carboxylic acid, 6,11-dihydro-3,8,9-trimethoxy-11-methyl-5-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:217316 CAPLUS

DOCUMENT NUMBER: 112:217316

TITLE: Benzophenanthridines. IX. Synthesis of  
11-methyl-C-norfagaronine chloride methyl ether from  
(±)-13α-hydroxyxylopinine

AUTHOR(S): Sazonova, N. M.; Sladkov, V. I.; Suvorov, N. N.

CORPORATE SOURCE: Mosk. Khim.-Tekhnol. Inst., Moscow, USSR

SOURCE: Zhurnal Organicheskoi Khimii (1989), 25(6), 1298-301

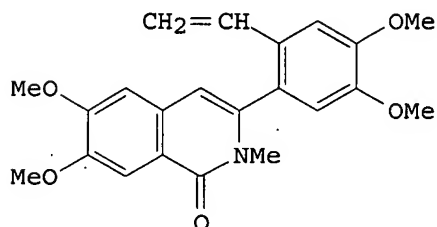
CODEN: ZORKAE; ISSN: 0514-7492

DOCUMENT TYPE: Journal

LANGUAGE: Russian

OTHER SOURCE(S): CASREACT 112:217316

GI



I

AB The title synthesis was carried out in 4 steps via Hofmann degradation of  
(±)-13α-hydroxy-Nα-methylxylopinine to the isoquinoline  
intermediate I, followed by acid-catalyzed cycloaddn. and then reduction with

10/553,532

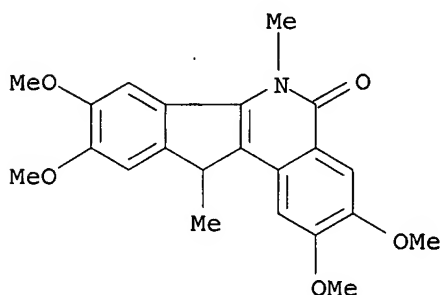
LiAlH<sub>4</sub>.

IT 125455-90-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reduction of)

RN 125455-90-5 CAPLUS

CN 5H-Indeno[1,2-c]isoquinolin-5-one, 6,11-dihydro-2,3,8,9-tetramethoxy-6,11-  
dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1968:49819 CAPLUS

DOCUMENT NUMBER: 68:49819

TITLE: Chemistry of cryptopine. I. The epicryptopines

AUTHOR(S): Dyke, Stanley F.; Brown, David Whitson

CORPORATE SOURCE: Bath Univ. Technol., Bristol, UK

SOURCE: Tetrahedron (1968), 24(3), 1455-65

CODEN: TETRAB; ISSN: 0040-4020

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB The chemistry of the epicryptopines, A (I), B and C, of the  
epimethylcryptopines A (II) and B and of epicryptopirubin chloride was  
reexamd., and some new structural proposals made.

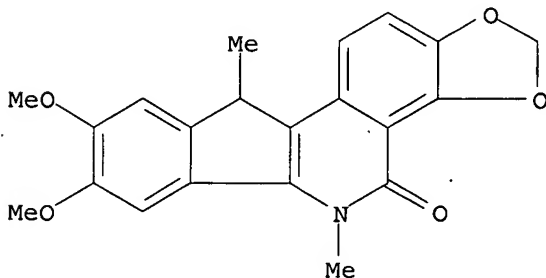
IT 18058-43-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 18058-43-0 CAPLUS

CN Epicryptopirubine, hydroxy-, chloride (8CI) (CA INDEX NAME)

Currently available stereo shown.



● HCl

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FILE 'REGISTRY' ENTERED AT 11:19:32 ON 31 OCT 2006

L1 STRUCTURE UPLOADED

L2 3 S L1

L3 48 S L1 FULL

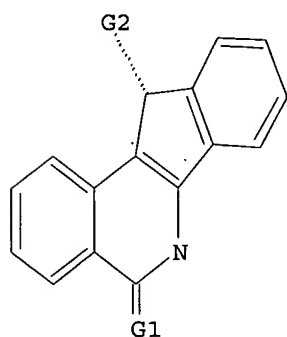
FILE 'CAPLUS' ENTERED AT 11:20:02 ON 31 OCT 2006

L4 19 S L3

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 O,S

G2 C,N

Structure attributes must be viewed using STN Express query preparation.

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